The opinion in support of the decision being entered today was not written for publication and is not precedent of the Board.

Paper No. 20

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES

Ex parte ALAN MCCLELLAND, SUSAN C. STEVENSON,
MARIO GORZIGLIA and ELIO VANIN

Appeal No. 2001-1053
Application 08/852,924

ON BRIEF

Before ROBINSON, SCHEINER and MILLS, Administrative Patent Judges.

MILLS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on appeal under 35 U.S.C. §134 from the examiner's final rejection of claims 2, 7, 9, 11-15 and 28, which are the claims on appeal in the application. Claims 19-26 have been withdrawn from consideration by the examiner and are not the subject of this appeal.

We affirm.

Claim 28 is illustrative of the claims on appeal and reads as follows:

28. A method of transferring at least one DNA sequence into cells selected from the group consisting of hematopoetic cells, head and neck cancer cells, neuroblastoma cells, lymphoma cells, leukemia cells, comprising:

transducing said cells with a modified adenovirus including said at least one DNA sequence, wherein said adenovirus, prior to modification, is Adenovirus 5, and wherein, in the modified adenovirus, at least a portion of the fiber of said Adenovirus 5 DNA is removed and replaced with at least a portion of the fiber of Adenovirus 3, and wherein said cells include a receptor which binds to said at least a portion of the fiber of Adenovirus 3, whereby transfer of said at least one DNA sequence into said cells is effected through binding of said modified adenovirus to said cells.

The prior art reference relied upon by the examiner is:

Wickham	5,770,442	June 23, 1998 (filed Feb, 21, 1995)

Reference relied on by the Appellants is:

Di Guilimi et al. (Di Guilimi), "Human adenovirus serotype 3 (Ad3) and the Ad3 fiber protein bind to a 130-kDa membrane protein on HeLa cells," Virus Research, Vol. 38, pp. 71-81 (1995)

Ground of Rejection

Claims 2, 7, 9, 11-15 and 28 stand rejected under 35 U.S.C. § 103(a) as obvious over Wickham.

Grouping of Claims

According to appellants, the claims stand or fall together. Brief, page 3. We decide this appeal on the basis of claim 28, as representative of claims 2, 7, 9, 11-15 and 28. 37 CFR §1.192(c)(7) (1996).

DISCUSSION

In reaching our decision in this appeal, we have given consideration to the appellants' specification and claims, to the applied prior art reference, and to the respective positions articulated by the appellants and the examiner.

Rather than reiterate the conflicting viewpoints advanced by the examiner and the appellants regarding the noted rejection, we make reference to the examiner's Answer for the examiner's reasoning in support of the rejection, and to the appellants' Brief, for arguments thereagainst. As a consequence of our review, we make the determinations which follow.

Claim Interpretation

Our appellate reviewing court stated in Panduit Corp. v. Dennison Mfg. Co., 810 F.2d 1561, 1567-1568, 1 USPQ2d 1593, 1597 (Fed. Cir.), cert denied, 481 U.S. 1052 (1987):

> Analysis begins with a key legal question -- what is the invention claimed? Courts are required to view the claimed invention as a whole. 35 U.S.C. 103. Claim interpretation, in light of the specification, claim language, other claims and prosecution history, is a matter of law and will normally control the remainder of the decisional process. [Footnote omitted.]

To that end, we also note that during ex parte prosecution, claims are to be given their broadest reasonable interpretation consistent with the description of the invention in the

specification. In re Zletz, 893 F.2d 319, 321, 13 USPQ2d 1320, 1322 (Fed. Cir. 1989).

In the present case, claim 28 is broadly interpreted as directed to any method of transferring at least one DNA sequence into cells selected from the group consisting of hematopoetic cells, head and neck cancer cells, neuroblastoma cells, lymphoma cells, leukemia cells. Thus, the method may be employed to transduce cells in vivo, ex vivo or in vitro. Specification, page 20. According to the specification, the method of the invention includes gene delivery. Specification, page 1.

Claim 28 does not recite any binding efficiency of the adenovirus to specific or generic cell types, and thus encompasses any binding of the adenovirus to the cell, however small. Nor does claim 28 require that the full adenoviral capsid fiber protein be present or participate in the attachment process of binding to the cell receptor. The claims merely recite that "at least a portion of the fiber of said Adenovirus 5 DNA is removed and replaced with at least a portion of the fiber of Adenovirus 3." Furthermore, there is no requirement in claim 28 that the act of binding to the cell receptor require only that the binding be performed by a portion of the fiber of Adenovirus 3, (i.e., the claims do not exclude that the binding of the portion of the adenovirus 3 fiber to the receptor may also include binding of the receptor to a remaining portion of the Adenovirus 5 fiber). With the above claim interpretation, we proceed to the prior art rejection of the claims.

35 U.S.C. § 103(a)

Claims 2, 7, 9, 11-15 and 28 stand rejected under 35 U.S.C. § 103(a) as obvious over Wickham.

In rejecting claims under 35 U.S.C. § 103, the examiner bears the initial burden of presenting a prima facie case of obviousness. See In re Rijckaert, 9 F.3d 1531, 1532, 28 USPQ2d 1955, 1956 (Fed. Cir. 1993). A prima facie case of obviousness is established when the teachings from the prior art itself would appear to have suggested the claimed subject matter to a person of ordinary skill in the art. In re Bell, 991 F.2d 781, 783, 26 USPQ2d 1529, 1531 (Fed. Cir. 1993). An obviousness analysis requires that the prior art both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. In re Vaeck, 947 F.2d 488, 493, 20 USPQ2d 1438, 1442 (Fed. Cir. 1991).

The examiner relies on Wickham as describing adenoviral vectors comprising a gene of interest and having a chimeric fiber protein comprising at least a head region derived from an adenovirus of a serotype other than used for the vector. "One such adenoviral vector disclosed is a chimeric Ad5 vector wherein at least the head (or knob) domain is derived from Ad3 - chimeric Ad3/Ad5 vector." Answer, page 3. Wickham also describes pharmaceutical compositions comprising such vectors and methods of using the vectors to transduce cells either in vitro or in vivo. Id. The examiner states that Wickham further discloses that "Ad5 vectors comprising Ad3 head domain have a much broader host cell range than Ad5 vectors have with their native fiber protein,

being able to infect essentially any higher eukaryotic cell. The reference teaches that the adenoviral vectors can be used to transduce cancer cells, e.g. lung, in treating hemophilia, which could involve hematopoeitic cells and in preventing restenosis, which would involve transducing smooth muscle cells, or to study the effects of expression of a transgene on a given cell-type in vitro and in vivo." Id.

Wickham states at column 12, lines 57-62, that

> The receptor for Ad3 contains a sialic acid component, which is required for binding of Ad3, while binding of Ad5 does not involve sialic acid. Since sialic acid is found on all higher eukaryotic cells, the Ad3/Ad5 fiber chimera is capable of binding to all cells. Such a vector can infect a broader range of cell types and exhibits different tissue specificity than non-chimeric Ad5 vectors in vivo. [Emphasis added.]

The examiner summarizes (Answer, page 4):

> Therefore, it would have been obvious to one skill in the art at the time the invention was made to use the method of Wickham et al of transduction with modified adenovirus vectors having chimeric fiber proteins, e.g. Ad5 vector with Ad3 head domain on the fiber protein, to transfer a DNA sequence into virtually any cell type with a reasonable expectation of success since the Ad3 domain allows infection of essentially all higher eukaryotic cell types, and for the reasons explicitly stated in the references as part of gene therapy or to study the effects of expression of a transgene on a given cell type in vitro or in vivo.

Where the prior art, as here, gives reason or motivation to make the claimed invention, the burden then falls on an appellants to rebut that prima facie case. Such rebuttal or argument can consist of any other argument or presentation of evidence that is pertinent. In re Dillon, 919 F.2d 688, 692-93, 16 USPQ2d 1897, 1901 (Fed. Cir. 1990) (en banc), cert. denied, 500 U.S. 904 (1991).

Appellants respond, arguing that Wickham does not discuss specific cell types that may be transduced with chimeric Ad5 vector having a fiber protein comprising Ad3 fiber sequences.

The examiner counters, arguing (Answer, pages 4-5) that

> Wickham also describes specific therapeutic applications involving using chimeric Ad5 vectors in general to deliver cytotoxic gene[s], such as treating glioma (a form of brain cancer, i.e. "head cancer") or restenosis (vascular smooth muscle cell proliferation) (col. 10, lines 4-17). Implicitly, since the object is to kill target cells, glioma or restenotic cells are to be transduced, and since Wickham teaches that Ad3/Ad5 chimeric fibers bind to all cells (col. 12, lines 59-60), implicitly the Ad3/Ad5 chimeric vector would have been seen as suitable for transfecting the desired target cells.

We agree with the examiner that Wickham would reasonably appear to suggest that the Ad3/Ad5 chimeric vector would have been seen as suitable for transfecting head and neck cancer cells or vascular smooth muscle cells, as claimed.

Appellants also argue that, contrary to the assertions of the examiner, a person of ordinary skill in the art would not conclude that a modified adenovirus, in which a portion of the fiber of Adenovirus 5 is removed and replaced with a portion of the fiber of Adenovirus 3, would infect essentially all higher eukaryotic cell types in general, and the cell types defined in claim 28, in particular. Brief, pages 3-4.

Appellants rely on DiGuilmi as evidence that "several proteins from purified HeLa cell membranes were shown to interact with the Adenovirus 3 fiber proteins, but the ability of these proteins to act in the Adenovirus 3 attachment process as the primary receptor was not shown in this report." Brief, page 4. Appellant further relies on the

specification pages 42 and 43, and Figure 6 as evidence that certain cells, such as human diploid fibroblast cells and human coronary artery endothelial cells, were refractory to infection by an adenovirus in which at least a portion of the fiber of Adenovirus 5 is removed and replaced with at least a portion of the fiber of Adenovirus 3. Brief, paragraph bridging pages 4-5. For these reasons, appellants conclude that Wickham does not even remotely suggest to one of ordinary skill in the art that such vectors may be used to transduce hematopoetic cells, head and neck cancer cells, neuroblastoma cells, lymphoma cells, leukemia cells and smooth muscle cells. Brief, pages 3 and 6.

The examiner responds to these arguments, suggesting "the results of Figure 6 only show that infection of these cell types was less efficient than other cell types, but that infection was still observed." Answer, page 6. We agree with the examiner's characterization of Figure 6. Because we have interpreted claim 28 to encompass any binding of receptor to at least a portion of the fiber of Adenovirus 3, however minor, Figure 6 and DiGuilimi do appear to reasonably suggest the binding and infection of the cell types which appellant characterizes as "refractory" to infection. Brief, page 5.

Furthermore, according to appellants, "Wickham did not recognize that, although Adenovirus 5 vectors can transduce many cells efficiently, certain cells have a low level of Adenovirus 5 receptor and thus are not transduced efficiently, but that certain cells have higher levels of the Adenovirus 3 receptor." Brief, page 5. Appellants conclude that only they have found that, "if one constructs a modified Adenovirus 5 vector,

wherein at least the head portion of the fiber is removed and replaced with at least the head portion of the Adenovirus 3 fiber, one can generate titers sufficient to provide for the efficient transduction of a variety of cells, yet such vectors can transduce cells having an Adenovirus 3 receptor." Id.

The examiner replies, that although appellants appear to argue unexpected efficiency of transfection results for the claimed cell types, appellants have failed to provide "comparative experimental evidence relating to the infection or transduction efficiency of any cell types in vivo or the specific and generic cell types recited in claim 28 in culture." Answer, page 7.

Again, we agree with the examiner that appellants have failed to present appropriate comparative evidence to overcome the prima facie case of obviousness established by the examiner. Nor do appellants' claims reflect an improved efficiency of transfection results relative to a control for the claimed cell types. Appellants have failed to provide sufficient evidence to rebut the examiner's evidence supporting a reasonable expectation of success using the claimed cells.

After evidence or arguments are submitted by the appellants in response to rejection based on obviousness, patentability is determined on the totality of the record, by a preponderance of evidence with due consideration to persuasiveness of the argument. On balance, we believe that the totality of the evidence presented by the examiner and appellants weighs in favor of finding the claimed invention obvious in view of the cited reference. We find the examiner has established on the record before

us that the cited references both suggest the claimed subject matter and reveal a reasonable expectation of success to one reasonably skilled in the art. The rejection of the claims for obviousness of the claimed invention is affirmed.

Other Issue

Although we find it unnecessary to comment at this time as the rejection of the examiner has been affirmed, should prosecution continue on the present application we recommend that the examiner reconsider the issue of enablement of the claims, in view of their broad claim scope, as interpreted herein. It would appear that the claim scope is broad enough to encompass gene therapy methods. The examiner should determine whether appellants' specification has provided enablement for gene therapy methods.

CONCLUSION

The rejection of claims 2, 7, 9, 11-15 and 28 under 35 U.S.C. § 103(a) as obvious over Wickham is affirmed.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED

Douglas W. Robinson
Administrative Patent Judge

Toni R. Scheiner
Administrative Patent Judge

Demetra J. Mills
Administrative Patent Judge

) BOARD OF PATENT
) APPEALS AND
) INTERFERENCES

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